Genetics

COMPARATIVE DNA SEQUENCING OF THE CODING REGIONS OF THREE QTL CANDIDATE GENES RELATED TO ALCOHOL ACTION. Rita Lee Strack, Erik MacLaren, Andrew Fortna and James M. Sikela*, University of Colorado Health Sciences Center, Denver CO 80262, james.sikela@uchsc.edu

Differential sensitivity to a hypnotic dose of ethanol has been used as a phenotypic marker in the development of selected inbred strains of mice (ILS and ISS) that have been widely studied as a model for alcohol action. Four chromosomal regions (QTLs) or *Lores* (loss of righting due to ethanol), have been identified that are thought to contain genes contributing to the differential alcohol sensitivity of these strains. Previously we have reported results of high throughput comparative gene sequencing of QTL-localized genes, as well as fine mapping of altered genes either within or out of narrowed QTLs intervals. Here we present a comparison between ILS and ISS mice of the coding sequences of three new *Lore* candidate genes: Pecr, Gpr73l1, and Atp1b2. These genes are located within *Lore1*, *2*, and *4* respectively.

One polymorphism was found between the ILS and ISS strains in Atp1b2 that is predicted to alter the amino acid sequence its protein product. Such a coding region SNP is a promising candidate to contribute to the alcohol sensitivity phenotype and merits additional study. Ten additional polymorphisms were found in these three genes that are not predicted to alter the proteins' sequences. These so-called "silent" SNPs are functionally unimportant, but can be used as genetic markers for the ILS and ISS strains. Lastly, two SNPs were found in Gpr73l1 that are shared between the two strains, but differ from the published nucleotide sequence of the gene. One of these changes is predicted to alter the ILS and ISS protein sequence compared to the published sequence.